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Task Force 6. Cost Effectiveness of Assessment and Management of Risk Factors

LEE GOLDMAN, MD, FACC, CHAIR, ALAN M. GARBER, MD, PHD,
STEVEN A. GROVER, MD, MPA, FRCPC, MARK A. HLATKY, MD, FACC

Cost-effectiveness analysis is a widely used method for determining the value of a health intervention. It seeks to determine the cost-effectiveness ratio, or the dollar cost per unit improvement in health obtained by a specific health intervention, in comparison with a well defined alternative intervention (1,2).

Cost-effectiveness analysis serves as an aid in selecting the clinical strategies that lead to the greatest health improvements for a given expenditure. It does so by estimating both the costs and health effects of alternative strategies, making explicit the dollar and health tradeoffs involved. Because these tradeoffs are ubiquitous within health care, affecting physicians, hospitals, health care systems, insurers, government programs and patients, cost-effectiveness analysis has gained wider use and is beginning to be used in some parts of the world as a means of deciding which drugs and other treatments are made available under national health plans. In the United States, the method is used to inform clinical guidelines and to market drugs and other forms of therapy; it is likely to be used increasingly in making decisions about insurance coverage.

Cost-effectiveness analysis is a method of considering both the effectiveness of an intervention and its cost. One major importance of cost-effectiveness is that it emphasizes the relevance of both components of the ratio and ensures that both effectiveness and cost are considered in clinical decision making.

The cost-effectiveness ratio is defined as the difference in costs between two interventions, divided by the difference in effectiveness, defined as years of life or quality-adjusted life years (QALYs):

$$CE_{2-1} = \frac{Cost_2 - Cost_1}{QALY_2 - QALY_1}.$$

Cost-effectiveness analysis should be distinguished from cost-benefit analysis. In cost-effectiveness analysis, the costs are commonly expressed in monetary terms, whereas the effectiveness is expressed as a health benefit, such as years of life saved or quality-adjusted years of life saved. By comparison, in cost-benefit analysis, both costs and benefits are expressed in the same terms, usually in dollars.

Cost-effectiveness analysis is a useful way to express the potential benefit to be gained from a particular investment. Because programs rarely save both costs and lives, the relative benefit achieved from one investment can be compared with what would be expected from another investment. Cost-effectiveness analysis is also a useful way for health planners to determine the maximal benefit that could be gained from a given amount of funds or to determine the lowest cost way to achieve a desired level of effectiveness. The method cannot find the greatest possible benefit for the lowest possible cost, because both cannot be obtained simultaneously.

Because a cost-effectiveness ratio is determined by dividing the change in total cost by the change in total health effectiveness, the same ratio may be obtained for programs with markedly different total costs and total benefits, provided that the ratios are the same. Thus, from a health policy perspective, it is important to understand not only the relative cost-effectiveness of an intervention, but also the total investment that would be required if it were to be applied to the target population.

Because cost-effectiveness analyses are driven by the validity of the assumptions on which their calculations are based, most analyses include a "sensitivity analysis," in which estimates are repeated using differing assumptions. If the message of the analysis is unchanged using reasonable variations in the relevant estimates, the reader can be more confident in the accuracy of its results.

Several additional issues must be addressed in any cost-effectiveness analysis. These include the perspective of the analysis, the alternatives to be compared, the measurement of health outcomes and the measurement of costs.

Perspective of the Analysis

To determine which costs should be included in a cost-effectiveness analysis, it is essential to describe at the outset whose perspective is being used; in other words, whose costs matter? An analysis conducted from the perspective of an individual patient who has traditional (indemnity-type) health insurance might incorporate only the costs that the patient bears directly, such as a 20% or even smaller copayment. An analysis conducted from the perspective of an insurer would include the insurance payments that the patient does not bear and would ignore the out-of-pocket payments. Neither of these

approaches incorporates all of the resources used to treat the patient. The most widely used and accepted perspective for conducting cost-effectiveness analysis is the *societal* perspective, which includes all costs and which avoids double counting. For example, disability insurance payments represent transfers from an insurer to the disabled claimant. Although the costs of administering such insurance are genuine costs, the transfer from the insurer to the patient is a cost to one and a benefit to the other, and should not be incorporated as a cost in an analysis conducted from the societal perspective.

Specifying the Alternatives

Every cost-effectiveness analysis implicitly or explicitly incorporates a comparison between two alternatives, with the expectation that the better option can then be compared with another until the best option has been described. The first alternative, and usually the one that motivates the analysis, is the intervention under study; it may be the use of a cholesterol-lowering drug, it may be sigmoidoscopy as a screening test for colon cancer, or it may be cardiac catheterization in an individual who has chest pain. The cost-effectiveness of any intervention depends crucially on the alternatives with which it is compared. One possible alternative is to "do nothing"; another is standard therapy. The former is an appropriate alternative only if it in fact represents a commonly used or otherwise justifiable approach. If we wish to consider the cost-effectiveness of coronary bypass surgery in patients with angina and three-vessel coronary artery disease, a cost-effectiveness analysis that compares bypass surgery with "do nothing" would not be informative, insofar as we believe that any symptomatic patient with documented coronary artery disease would be treated with drugs or an alternative revascularization procedure.

Once the intervention and the alternative have been selected, it should be recognized that the numerator of the cost-effectiveness ratio, which is described in greater detail later, is the difference in costs between the two interventions, not the cost of the intervention under primary consideration by itself. Similarly, the denominator of the cost-effectiveness ratio is the difference in health effects between the intervention and the alternative. Thus, cost-effectiveness analysis is always comparative, in the sense that the numerator consists of the amount by which the health care costs of patients receiving the intervention differs from the costs of patients receiving the alternative, and the denominator consists of the amount by which the intervention changes the health outcome.

Measuring Health Effects

To be useful, cost-effectiveness analysis must include a measure of health effects or health outcomes based on the aspects of health that patients care about. Thus, for example, the effectiveness measure ordinarily should not be the cost per positive test (for a diagnostic or screening test) or the cost per unit change in blood pressure, unless there is a direct link between these intermediate outcomes and "final outcome." Furthermore, the measures should be sufficiently global to make it possible to compare different kinds of health interventions and sufficiently sensitive as a measurement instrument to capture changes in health that patients can detect and lead to an appreciable improvement in their quality of life or sense of well-being. Traditionally, the most widely used global health outcome measure had been life expectancy, which is readily measured, easily interpreted and can be used to compare a wide range of interventions. The major drawback of using life expectancy as the only outcome measure is that it does not account for any changes in the quality of life. Particularly for interventions that relieve pain or improve functional status, life expectancy is an inadequate measure of health effects.

The outcome measure that has gained the greatest acceptance, at least on a conceptual level, is quality-adjusted life years or, as it is sometimes called, quality-adjusted life expectancy. This measure is analogous to life expectancy but gives less "credit" to years of life that are spent in pain, impaired health or diminished function. An intervention that improves quality of life can generate an increase in quality-adjusted life years, even if it has no effect on the duration of survival. Similarly, an intervention that lengthens life produces more quality-adjusted life years if it maintains or improves quality of life than if it adds years of life that are impaired by significant morbidity. A large literature discusses alternative measures of quality of life that can be incorporated into the quality-adjusted life year measure, and although there is not yet consensus about the best measure of quality-adjusted life years to use, there is widespread agreement that it is conceptually appropriate to perform the quality adjustment and use quality-adjusted life years, or something akin to quality-adjusted life years, as an outcome measure in cost-effectiveness studies.

In the calculation of effectiveness, both the risks and benefits of the intervention must be considered. For example, the potential side effects of aspirin may outweigh its benefits in patients who are at low risk for ischemic vascular disease but at higher risk for intracerebral or gastrointestinal bleeding. Obviously an intervention will become less attractive from a cost-effectiveness standpoint if, in the overall population or in identifiable subgroups, its risks largely or fully counterbalance its benefits.

Measuring Costs

All cost-effectiveness analyses of medical treatments generally include any direct medical costs related to the diagnosis and treatment of the disease under question as well as any disease-specific costs that may be induced or averted. For example, a cost-effectiveness analysis of cholesterol reduction must include the cost of the therapy and consider any cardiac-related costs that may be avoided or added. Many analyses also include other medical costs unrelated to the specific disease in question. In the preceding example, such costs might include the cost of cancer or stroke in patients whose fatal heart disease was averted because of cholesterol reduction. More

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complicated and controversial analyses also include costs that are not purely medical, such as the cost of nursing home care for an elderly person whose life was prolonged because of cholesterol reduction. Even more controversial are analyses that include calculations for lost earnings, lost opportunities or societal transfers, such as social security or disability payments.

Many health care institutions are developing sophisticated cost-accounting methodologies that attempt to assign unit costs rather than charges to individual services. In the calculation of medical costs, it is sometimes quite difficult to distinguish fixed costs, which do not depend on the volume of services, from variable costs, which may be critically dependent on volume and diminish for the marginal case.

Discounting

In cost-effectiveness analysis, costs and benefits in the future are not as highly valued as costs or benefits that may be realized immediately. To adjust for the diminished value of future costs and benefits, analyses use the principle of discounting. In addition to recognizing the preference to postpone costs but realize the benefit immediately, discounting also takes into account the possibility that other diseases or medical breakthroughs may intervene and partially or fully negate the expected future benefit from the screening or preventive intervention. Although a substantial theoretical literature has debated whether the discount rate should be linked to the rate of monetary inflation, analyses generally discount future costs and benefits by about 3% to 5% per year. The principle of discounting explains why screening and preventive strategies can be very costly if the expenses must be borne immediately, whereas the benefits may not accrue for many years.

Cost-Effectiveness of Screening

Many commonly used screening tests and procedures are inexpensive, yet the total cost of a screening program includes not only the initial screening test, but all the costs induced by the actions that follow a test result. The first recommendations of the Adult Treatment Panel of the National Cholesterol Education Program, for example, called for all adults to undergo testing with a total blood cholesterol level once every 5 years. The per-person cost of such testing is quite modest. However, individuals found to have an undesirably high blood cholesterol level, according to these recommendations, would undergo further testing, detailed evaluation and, for those deemed to be at high risk, dietary counseling and, in some cases, treatment with drugs. Although each step of this cascade of management involves fewer and fewer people, the costs typically rise. For example, for the first recommendation of the original National Cholesterol Education Program's Adult Treatment Panel Cholesterol Guidelines, the screening tests themselves would account for approximately one-fortieth of the entire costs of implementing the program. Thus, even though every participant in a screening program generates costs from the initial screening tests, the costs of treating the minority who need drugs account for most of the costs of the screening program (3).

Treatment also plays a crucial role in the cost-effectiveness of the screening program. The cost-effectiveness of screening for any risk factor or occult disease is closely related to the cost-effectiveness of its treatment. Typically, cost-effectiveness analyses of treatment assume that the individuals with the risk factor or disease (i.e., the candidates for treatment) have already been identified. All efforts and associated costs of identifying them were incurred in the past, and are no longer relevant to the treatment decision. However, those costs are central to analyzing the cost-effectiveness of screening programs, which begin with the process of identifying such individuals. The cost-effectiveness of a screening program is limited by the cost-effectiveness of subsequent treatment; ordinarily all of the benefits of screening result from the treatment, so there are no additional benefits from the screening program, yet screening itself imposes costs that are ignored in an analysis of treatment. If treating a person with a known cholesterol level is not cost-effective, it cannot be cost-effective to screen that person.

The cost-effectiveness of screening depends on several factors besides the cost-effectiveness of treatment. These factors include the test's ability to discriminate between people who do and do not have the disease or risk factor (sensitivity and specificity), the cost of the test as well as any risks or health benefits directly resulting from the testing procedure (which are negligible for many screening tests) (4,5).

The estimation of costs is, by definition, subject to uncertainties and future changes. For example, medications may become less expensive when their patents expire, if and when the availability of multiple medications in the same class provides price competition, or if large purchasers can demand lower prices. Reductions in the costs of cardiac care, driven by managed care and competition, may actually make prevention somewhat less attractive economically since future savings, generated by avoiding or delaying future events, are reduced.

Influence of Other Risk Factors on the Costs and Benefits of Risk Reduction

The cost-effectiveness of risk factor modification is extremely sensitive to the presence of known coronary heart disease or other risk factors. For instance, the cost-effectiveness ratios of secondary prevention are usually forecasted to be superior to those of primary prevention. Individuals with preexisting disease have a substantially increased risk of dying from coronary disease compared with those without coronary heart disease (6,7). Accordingly, the short-term benefits of modifying one or more risk factors should be associated with a greater absolute risk reduction in secondary prevention compared with primary prevention. The presence of coronary heart disease also significantly decreases one's life expectancy. Therefore, the time horizon for therapy is shortened, resulting in lower costs associated with risk factor modification for

Table 1. Example of Costs, Effectiveness and Cost-Effectiveness for a Hypothetical Intervention in 10,000 Patients for 5 Years* (high risk patients versus low risk patients)

	High Risk		Low Risk	
	Untreated	Treated	Untreated	Treated
Annual death rate	10%	5%	1%	0.5%
Yr of life saved†	0	5,209	0	614
Cost of treatment ($ millions) at $2,000/yr	0	90.5	0	99.0
Annual CABG rate	6%	3%	0.6%	0.3%
Cost/CABG	$20,000	$20,000	$20,000	$20,000
Annual MI rate	4%	2%	0.4%	0.2%
Cost/MI	$10,000	$10,000	$10,000	$10,000
Annual rate of other events	4%	2%	0.4%	0.2%
Cost/other event	$5,000	$5,000	$5,000	$5,000
Medical costs ($ millions)	70.0	39.7	8.8	4.4
Total cost ($ millions)	70.0	130.2	8.8	103.4
Total cost difference ($ millions)		60.2		94.8
Approximate cost/yr of life saved		$11,500		$155,000

*Simplified so that the intervention reduces all risks by 50%, neither costs nor health effects discounted, all patients are assumed to die at midyear, and the analysis considers only the first 5 years. †By life-table analysis. CABG = coronary artery bypass graft surgery; MI = myocardial infarction.

secondary versus primary prevention. All other things being equal, secondary prevention should be associated with greater short-term benefits and lower long-term costs, resulting in superior cost-effectiveness ratios compared with primary prevention. As more and more sensitive measures are found to identify currently preclinical coronary artery disease, the risk of future events and hence the cost-effectiveness of treatments can be expected to be somewhere in between current forecasts for secondary and primary prevention.

The overall effectiveness of an intervention is generally greater in high risk patients because

$$\text{Absolute risk reduction} = \text{Underlying risk} \times \text{Relative risk reduction.}$$

These principles can be illustrated by a hypothetical example. Suppose an intervention can be given to either high or low risk patients, at a cost of $2,000/year for 5 years. If the drug reduces death and cardiac events by 50%, its cost-effectiveness depends on the underlying (or baseline) risk in the population being treated (Table 1). To illustrate this principle, Goldman et al. (8) estimated the cost-effectiveness of HMG-CoA reductase inhibition for primary and secondary prevention of coronary heart disease. When used for secondary prevention, 20 mg/day of lovastatin was estimated to save lives and money in younger men with cholesterol levels above 250 mg/dl, and to be cost-effective for all other patients except young women with cholesterol levels below 250 mg/dl. However, in primary prevention, favorable cost-effectiveness ratios were forecasted only for select subgroups among whom cholesterol levels were extremely high, such as in patients with heterozygous familial hypercholesterolemia (9), or in whom very high (usually above 300 mg/dl) cholesterol levels were accompanied by other coronary risk factors.

The presence of multiple risk factors for coronary disease also makes the cost-effectiveness ratios of risk factor modification more favorable for reasons similar to those described in secondary prevention. Multiple risk factors place an individual at high absolute risk of coronary events, so modification of any one risk factor (i.e., cigarette smoking, hyperlipidemia, hypertension) is therefore associated with a greater decrease in absolute coronary risk. For instance, Hamilton et al. (10) estimated that lipid modification among Canadian adults with pretreatment cholesterol levels above the 90th percentile of the U.S. distribution in this age group would cost $34,000 (in 1993 U.S. dollars) per year of life saved among low risk men compared with $16,000 among high risk men who smoke cigarettes and have hypertension. These results were consistent with those of Goldman et al. (8), where lipid modification among American men 45 to 54 years old with pretreatment cholesterol levels of 300 mg/dl or higher would cost about $130,000 (in 1993 dollars) per year of life saved in the absence of coronary risk factors but only about $15,000 in the presence of diastolic hypertension, cigarette smoking and obesity. For antihypertensive therapy, Lindgren and Persson (11) have estimated that heavy cigarette smoking would improve the cost-effectiveness ratios of antihypertensive therapy for a 52-year old Swedish man by 25% or more.

It should be emphasized that all of these analyses estimated changes in life expectancy based on the multivariate logistic equations developed by the Framingham Heart Study (12). There remains some disagreement as to whether or not these independent risk factors are multiplicative or additive in nature. The cost-effective estimates described assumed the multiplicative relationship, which will increase the importance of multiple risk factors.

Hyperlipidemia

Screening. The cost-effectiveness of cholesterol screening is likely to be similar to the cost-effectiveness of treatment because treatment, not testing, is responsible for most of the costs of cholesterol screening programs (3). Nevertheless, because most of the published estimates of the cost-effectiveness of treatment excluded the costs of the screening tests, the cost per life-year saved for a screening and treatment program are, by definition, somewhat higher than the published estimates for treatment programs alone.

Treatment. Among specific modifiable risk factors, hyperlipidemia has been the most comprehensively studied from a health economics perspective. The majority of these studies draw heavily on the results of the Framingham Heart Study, as the benefits associated with lipid modification are usually based on these published univariate and multivariate regression equations (7,13,14).

As is standard in cost-effectiveness analysis, the authors of studies of cholesterol reduction measured the costs of the

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intervention (typically a drug or diet), the savings resulting from the prevention of myocardial infarction and other manifestations of coronary heart disease, and the costs of any diseases or health conditions that result from treatment. The "net costs" of the intervention comprise the numerator of the cost-effectiveness ratio; the denominator is the increase in the life expectancy that results from treatment. Nearly all published studies of the cost-effectiveness of treatment make the crucial assumptions that cholesterol reduction reduces coronary heart disease incidence and does not increase morbidity or death from any other causes (15). The cholesterol-lowering intervention reduces some future medical expenditures and increases life expectancy by preventing coronary heart disease. If the assumption that treatment has a negligible effect on morbidity and death from other causes is incorrect, such studies both underestimate the costs of the intervention (by ignoring the costs of treating diseases that the intervention promotes) and overestimate the beneficial health effects.

Overall, the results of these analyses are reasonably similar, with more favorable cost-effectiveness ratios forecasted for high risk individuals compared with those at low risk (15–18). Treatment of hyperlipidemia is also usually predicted to be more cost-effective for men than women because of the relatively higher absolute risk of coronary disease among men, all else being equal.

Weinstein and Stason (19) and Goldman et al. (8,9) have published a number of analyses on the cost-effectiveness of lipid modification. Early estimates by Weinstein and Stason (19) were based on the results of the Lipid Research Clinics Trial and focused only on men 45 to 50 years old with a serum cholesterol greater than 265 mg/dl. Assuming annual treatment costs of $2,000 and full compliance, they estimated a cost per year of life saved of over $175,000 for cholestyramine in 1993 dollars. Later work, using the Coronary Heart Disease Policy Model, also included the cost savings of preventing nonfatal coronary events and estimated the cost-effectiveness of HMG-CoA reductase inhibition for primary and secondary coronary heart disease prevention (8). Primary prevention in men with pretreatment cholesterol levels of 300 mg/dl (7.76 mmol/liter) or higher was associated with cost-effectiveness ratios ranging from about $15,000 to about $350,000 per year of life saved in 1993 dollars. The least favorable cost-effectiveness ratios were found among young men without other risk factors. More favorable cost-effectiveness ratios were estimated for middle-aged men 45 to 64 years old with multiple risk factors, including hypertension, cigarette smoking and obesity. The results for women were substantially higher, ranging from about $1.75 million per year of life saved to about $40,000 per year of life saved in 1993 dollars. As previously mentioned, this analysis also forecast overall cost savings associated with secondary prevention in men 35 to 54 years old and very favorable cost-effectiveness ratios for most individuals with clinically evident coronary disease.

Oster and Epstein (18) used data from the Lipid Research Clinics Trial to estimate the cost-effectiveness of cholesterol reduction associated with cholestyramine. Among men 35 to 74 years old, the cost-effectiveness of lifelong therapy ranged from about $95,000 to over $1.75 million per year of life saved in 1993 dollars. Younger individuals and those with higher pretreatment cholesterol levels had more favorable cost-effectiveness ratios. Their analyses also suggested that midterm therapy (i.e., 20 years) may be more cost-effective than lifelong therapy. Once again, treatment was more cost-effective for individuals with multiple risk factors. For instance, the cost-effectiveness ratios for men of all ages with smoking, hypertension and diabetes were less than 50% of the values calculated for those who had no additional risk factors other than their hyperlipidemia. It should be noted that this study also included an estimate of the medical care costs associated with noncardiovascular diseases resulting from patients living longer.

Using data from the Lipid Research Clinics Trial, Kinosian and Eisenberg (17) estimated the cost-effectiveness of cholestyramine resin, colestipol and oat bran. The cost per year of life saved was estimated at about $160,000 for cholestyramine resin, about $95,000 for colestipol and about $23,000 for oat bran (in 1993 dollars) when applied to the Lipid Research Clinics Trial cohort (i.e., men, mean age 48 years, pretreatment cholesterol greater than 6.85 mmol/liter [265 mg/dl]). Once again, cost-effectiveness ratios were more favorable if the intervention was targeted only at those individuals with additional risk factors. This analysis also estimated a 20% reduction in cost-effectiveness ratios for drug therapy when the indirect savings associated with lost earnings were considered for those who become unemployed as a result of coronary disease.

Hay et al. (16) incorporated the indirect benefits of reduced disability days associated with coronary heart disease into their economic evaluation of lovastatin for coronary heart disease prevention. For this and perhaps other reasons, this analysis predicted some of the most favorable cost-effectiveness ratios to date, ranging from about $11,000 to $130,000 (in 1993 dollars) for the average-risk man and from about $40,000 to $360,000 for the average-risk woman. The cost-effectiveness ratios for high risk individuals were improved to as little as about $7,500 per year of life saved for men and about $23,000 for women.

The previously described models estimated the benefits of reducing total cholesterol, but high density lipoprotein (HDL) cholesterol levels could have a substantial impact on the cost-effectiveness of lipid modification if the HDL effect is taken into account (15). Hamilton et al. (10) recently estimated that the cost-effectiveness ratios associated with HMG-CoA reductase inhibitors may be improved by approximately 40% if the HDL effect is considered. Using 20 mg of lovastatin as an example, this study forecast that a 7% increase in HDL, added to the expected 17% reduction in total cholesterol, would substantially improve the cost-effectiveness of this therapy. For instance, for low risk men between the ages of 30 and 70, the cost per year of life saved ranged from $50,000 to $170,000 (1993 dollars) without consideration of the HDL effect. However, when the HDL effect was considered, these ratios im-

proved to between $30,000 and $60,000 per year of life. The impact of the HDL effect was greatest for elderly individuals because of the diminishing relative risk associated with total cholesterol in the elderly.

Given the increasing awareness of the importance of serum lipids as modifiable coronary risk factors, one can anticipate continuing economic evaluations in this area. Future studies must include validation of statistical models wherever possible. For instance, Grover et al. (20) have used clinical trial results in one study to validate the accuracy of a primary prevention model. Additional work is also required to estimate the indirect cost savings associated with improved productivity among those in whom coronary events are presented. Also, quality of life assessments should be incorporated into existing models to support cost-utility analyses that better capture the improvements in mortality and morbidity associated with coronary heart disease prevention.

Hypertension

Screening. Screening for hypertension is highly cost-effective because blood pressure measurement, when done as part of an office visit for other purposes or in many other settings, is very inexpensive, and treatment of elevated blood pressure can be highly cost-effective. Littenberg et al. (21) estimated that screening cost approximately $18,500 per quality-adjusted life-year saved, in 1993 dollars, for men 40 years of age; the cost per quality-adjusted life-year was lower for older men and higher for women and younger men.

Hypertension is a particularly appropriate condition for screening because it usually causes no symptoms; the screening test is simple, safe and convenient; and available treatments are both inexpensive and highly effective. Much of the benefit of treating high blood pressure comes from improvements in quality of life, particularly those that result from stroke prevention, but treatment also reduces mortality. These effects are largest among people who have the greatest elevations of blood pressure, most of whom can be identified only by blood pressure testing.

Treatment. The cost-effectiveness ratio for the treatment of hypertension is generally favorable for men and women of all ages. Littenberg et al. (21) estimated that the marginal cost per quality-adjusted year of life gained ranged from about $33,000 for men at age 20 to about $9,000 for men at age 60 in 1993 dollars. For women, the cost ranged from about $50,000 per quality-adjusted year of life at age 20 to about $14,000 at age 60. The results of the analysis were dependent on the cost of medication but were relatively unaffected by other assumptions in the analysis.

Using data from the Framingham Heart Study, Weinstein and Stason (22) calculated that savings by avoiding strokes and coronary events would offset 20% to 25% of the cost of treating moderate to severe hypertension and about 15% of the cost of treating mild hypertension. Littenberg et al. (21) estimated that the cost per year of life saved was about $23,000 (in 1993 dollars) for moderate to severe hypertension and about twice as much for mild hypertension.

Edelson et al. (23) reported that primary prevention for diastolic blood pressures of 95 mm Hg or above without coronary heart disease in persons 35 to 60 years old cost about $14,000 per year of life saved for propranolol and about $20,000 for hydrochlorothiazide in 1993 dollars. Cost-effectiveness ratios varied widely for different medications and were estimated to range from about $60,000 to $90,000 per year of life saved for newer, more expensive medications.

Smoking

Cigarette smoking is a strong, consistent risk factor for the development of coronary heart disease. Since smoking can be completely eliminated, interventions to promote smoking cessation have greater potential for reducing cardiovascular risk than interventions on any other risk factor. Furthermore, since smoking is also a strong risk factor for lung and other cancers as well as for chronic obstructive lung disease, reduction of smoking would be expected to lower both noncardiac and cardiac mortality substantially.

The cardiovascular risk associated with smoking declines sharply in the first 6 months after smoking cessation and reaches the level of nonsmokers after 1 to 2 years. Risk appears to be reduced in both men and women and in both old and young patients. Because some of the risk of smoking appears to be mediated through enhanced thrombogenicity and coronary vasoconstriction, beneficial effects of smoking cessation can be expected even in patients with established atherosclerosis.

Life expectancy appears to be increased substantially in patients who quit smoking. Tsevat and co-workers (24) estimated that a 35-year old smoker would live 2.4 to 2.8 years longer if he or she stopped smoking. Taylor and colleagues (25), using a different model, estimated that life expectancy would be extended by 5.3 years in a 40-year old man who quit smoking and by 3.1 years in a 40-year old woman who quit smoking.

The effectiveness of interventions to promote smoking cessation is relatively low, since smokers are both addicted to nicotine and psychologically dependent on smoking. A meta-analysis of various smoking interventions suggested that an average of 5.8% (confidence interval 3.2% to 8.4%) more patients than control subjects will cease smoking 12 months after an intervention program (26).

Given their relatively modest cost, however, interventions against smoking appear very cost-effective. Cummings and colleagues (27) calculated that a physician's advice to stop smoking had a cost-effectiveness ratio of between about $1,000 to about $1,400 per year of life saved in men (1993 dollars) and between about $1,700 and $3,000 per year of life saved in women, depending on the patient's age. These investigators estimated that a physician's advice would still be cost-effective even with net smoking cessation rates as low as 1% at 1 year (their best estimate of the actual effect was 2.7% at 1 year). Oster and co-workers (28), in a similar analysis, estimated the

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cost-effectiveness of nicotine gum to range from about $6,000 to $9,000 for men and about $9,500 to $13,000 for women, in 1993 dollars, depending on age.

Interventions to promote smoking cessation appear to be highly cost-effective because of large potential gains in life expectancy among individuals who stop smoking. Smoking cessation programs are especially worth the cost when aimed at persons who already have coronary disease, such as patients who have survived a myocardial infarction (29,30).

Exercise and Cardiac Rehabilitation

The potential cost-effectiveness of cardiac rehabilitation, including exercise, for secondary prevention is based primarily on the estimates of two overview analyses of randomized trials in the 1980s (31,32). Using costs and efficacy data from a randomized clinical trial of cardiac rehabilitation, Oldridge and colleagues (33) completed an economic evaluation of cardiac rehabilitation after acute myocardial infarction. Patient mortality and morbidity were similar at 1 year between the control and intervention groups. However, quality of life, as measured by the time tradeoff method, demonstrated that a comprehensive cardiac rehabilitation program was associated with 0.052 quality-adjusted life years gained during the 1 year follow-up period. Given the incremental direct costs of a rehabilitation program, this resulted in costs per quality-adjusted life year gained of about $10,000. Incorporating estimated improvements in longevity from a meta-analysis of cardiac rehabilitation, the authors also forecast 0.022 additional years for cardiac rehabilitation patients over a 3 year follow-up period. Combining both reduced mortality over 3 years and improved quality of life in year 1, the cost per quality-adjusted life year gained due to rehabilitation was estimated at less than $8,000 in 1993 dollars.

There is even less sound data on primary prevention, and one can only speculate on the potential cost-effectiveness of exercise interventions in primary prevention. However, aerobic fitness is associated with positive effects on serum lipids, blood pressure, obesity and glucose intolerance (34–38), so the potential impact of modifying these multiple risk factors with one intervention could be extremely cost-effective. Moreover, lack of exercise in and of itself appears to be an independent risk factor for coronary disease even after adjustment for the secondary effects of physical fitness on other coronary risk factors.

Estrogen

The risk of coronary heart disease is very low in women until menopause, when it begins to rise progressively with age. This observation suggests that endogenous production of estrogen may either protect against the development of coronary atherosclerosis or prevent plaque rupture and coronary thrombosis, or both.

Observational studies comparing women taking postmenopausal estrogen therapy with control subjects have shown striking reductions in the rate of clinical coronary heart disease. Interpretation of these findings has been confounded by the generally healthier life-styles of women who take estrogen, including less smoking, more exercise and greater access to medical care. Randomized trials currently under way (the Heart Estrogen-Progestin Replacement Study and the Women's Health Initiative) will test the hypothesis that hormone replacement reduces the risk of heart disease in postmenopausal women.

The effect of estrogen replacement on life expectancy is complex. Hormone therapy appears to reduce the risk of osteoporosis and of hip fracture, as well as reduce the risk of coronary heart disease. Unfortunately, hormone therapy also appears to increase the risk of endometrial cancer and possibly breast cancer, although the latter finding remains controversial. The overall impact on life expectancy therefore depends on the balance of potential risks and benefits. Grady and colleagues (39) estimated that estrogen therapy in an average white 50-year old woman will increase life expectancy by 0.9 years. The potential benefit was 2.1 years in women with established coronary disease and 1.5 years in women at high risk for coronary heart disease. Women at high risk for breast cancer had less estimated benefit from estrogen therapy, with life expectancy increased by only 0.7 years. Thus, potential benefits of estrogen therapy vary according to clinical characteristics.

Cost-effectiveness analyses of estrogen therapy have been performed, but have not incorporated possible effects on coronary heart disease (40). Because the greatest potential gains in the life expectancy are due to the likely effects of estrogen on heart disease, previous cost-effectiveness analyses are likely to have underestimated the value of estrogen therapy.

Aspirin

Both oral anticoagulants and aspirin have been shown to be beneficial for reducing mortality after acute myocardial infarction. Based on its efficacy and economics, aspirin appears to be associated with favorable cost-effectiveness estimates and to be the preferred treatment unless a patient cannot tolerate it (41).

Cost-Effectiveness in Perspective

Cost-effectiveness analysis is intended to improve clinical practice and aid in the development of clinical guidelines and health policy by providing information about the value of alternative health interventions in specific populations. It is not intended to be the sole basis for resource allocation in health care because of technical limitations of the method and the importance of considerations that are not part of the analysis (such as specific social goals and local factors).

Results of cost-effectiveness analyses are often displayed in a comparative format called a "league table" (Table 2). League tables run the risk of including studies with differing assumptions. In updating results to a common year, the tables also make simplifying assumptions regarding inflation. Neverthe-

Table 2. Heart Disease Cost-Effectiveness Overview*

Strategy	Condition	Patient Targeting	Study (ref. no.)	Year	$/YLS or $/QALY†
		Highly Cost-Effective (<$20,000/YLS or QALY)			
Lovastatin (20 mg/d)	Hyperlipidemia	2°, chol ≥250 mg/dl, men 45–54 yr old	Goldman et al. (8)	1991	Saves $ and lives
Enalapril	CHF	EF ≤0.35	Glick et al. (42)	1994	Saves $ and lives
Nurse counseling manual	Smoking	Post-MI	Krumholz et al. (30)	1993	250
Physician counseling	Smoking	Men 50–54 yr old	Cummings et al. (27)	1989	1,300
Beta-blocker	Post-MI	High risk	Goldman et al. (43)	1987	3,600
Lovastatin (20 mg/d)	Hyperlipidemia	2°, chol ≥250 mg/dl, women 45–54 yr old	Goldman et al. (8)	1991	4,700
PTCA	Chronic CAD	Severe angina, 1 VD‡	Wong et al. (44)	1990	8,700–10,200†
CABG	Chronic CAD	Severe angina, left main disease§	Weinstein and Stason (45)	1982	9,200†
Advice and nicotine gum	Smoking	Women 50–54 yr old	Cummings et al. (27)	1989	13,000
Propranolol	Hypertension		Edelson et al. (23)	1990	16,900
Usual care	Hypertension	Women 60 yr old	Littenberg et al. (21)	1990	18,000†
CABG	Chronic CAD	Mild angina, 3 VD‖	Weinstein and Stason (45)	1982	18,200†
		Relatively Cost-Effective ($20,000–$40,000/YLS or QALY)			
Beta-blocker	MI	Low risk	Goldman et al. (43)	1987	20,200
Lovastatin (20 mg/d)	Hyperlipidemia	1°, chol ≥300 mg/dl, 3 RF, men 55–64 yr old	Goldman et al. (8)	1991	20,200
Exercise	Prophylaxis	Men 35 yr old	Hatziandreu et al. (46)	1988	22,400†
Lovastatin (20 mg/d)	Hyperlipidemia	2°, chol <250 mg/dl, men 55–64 yr old	Goldman et al. (8)	1991	22,900
Usual care	Hypertension	Men 40 yr old	Littenberg et al. (21)	1990	23,700†
Hydrochlorothiazide	Hypertension		Edelson et al. (23)	1990	25,400
Captopril	Post-MI	EF ≤0.40	Tsevat et al. (47)	1995	28,400†
Community-wide screening	Hypertension	DBP ≥105 mm Hg	Weinstein and Stason (45)	1976	29,700
ECG Ex testing	CAD	CAD, p = 0.60, men 55 yr old	Doubilet et al. (48)	1985	30,200†¶
Oat bran	Hyperlipidemia	LRC-CPPT Pt#	Kinosian and Eisenberg (17)	1988	31,600
CCU	Possible MI	MI, p = 0.50	Fineberg et al. (49)**	1984	35,000
Angiography	CAD	CAD, p = 0.90, men 55 yr old	Doubilet et al. (48)	1985	37,000†¶
ECG Ex testing	Asymptomatic	Men 60 yr old, ≥1 RF	Sox et al. (50)	1989	37,700
		Borderline (>$40,000–$60,000)			
Lovastatin (20 mg/d)	Hyperlipidemia	1°, chol ≥300 mg/dl, 2 RF, men 55–64 yr old	Goldman et al. (8)	1991	41,800
Usual care	Hypertension	DBP 95–104 mm Hg	Weinstein and Stason (22)	1976	41,900
CABG	Chronic CAD	Severe angina, 2 VD‖	Weinstein and Stason (45)	1982	42,500†
Usual care	Hypertension	Men 20 yr old	Littenberg et al. (21)	1990	42,600†
Lovastain (20 mg/d)	Hyperlipidemia	2°, chol <250 mg/dl, women 55–64 yr old	Goldman et al. (8)	1991	48,600
Nifedipine	Hypertension		Edelson et al. (23)	1990	48,900
		Expensive (>$60,000–$100,000/YLS or QALY)			
Usual care	Hypertension	Women 20 yr old	Littenberg et al. (21)	1990	64,500†
Angiography	CAD	CAD, p = 0.60, men 55 yr old	Doubilet et al. (48)	1985	71,300†¶
CABG	Chronic CAD	Severe angina, 1 VD‖	Weinstein and Stason (45)	1982	72,900†
CABG	Chronic CAD	Mild angina, 2 VD‖	Weinstein and Stason (45)	1982	72,900†
Lovastatin (20 mg/d)	Hyperlipidemia	1°, chol ≥300 mg/dl, 0 RF, men 55–64 yr old	Goldman et al. (8)	1991	78,300
CCU	Possible MI	MI, p = 0.20	Fineberg et al. (49)	1984	88,700
PTCA	Chronic CAD	Mild angina, 1 VD (CAD)	Wong et al. (44)	1990	91,500†

Table 2. Continued

Strategy	Condition	Patient Targeting	Study (ref. no.)	Year	$/YLS or $/QALY†
		Expensive (+$75,000/YLS or QALY)			
PTCA	Chronic CAD	Mild angina, 2 VD	Wong et al. (44)	1990	109,000†
Captopril	Hypertension		Edelson et al. (23)	1990	111,600
Cholestyramine bulk drug	Hyperlipidemia	LRC-CPPT Pt#	Kinosian and Eisenberg (18)	1988	115,500
Cholestyramine	Hyperlipidemia	Chol 315 mg/dl, 45–49 yr old	Oster and Epstein (17)	1987	122,100
ECG Ex testing	Asymptomatic	Men 40 yr old	Sox et al. (50)	1989	124,400
Lovastatin (20 mg/d)	Hyperlipidemia	1°, chol ≥300 mg/dl, 0 RF, men 45–54 yr old	Goldman et al. (8)	1991	148,500
CCU	Possible MI	MI, p = 0.10	Fineberg et al. (49)	1984	177,400
CCU	Possible MI	MI, p = 0.05	Fineberg et al. (49)	1984	373,800
CABG	Chronic CAD	Mild angina, 1 VD‖	Weinstein and Stason (45)	1982	1,142,000†
Cholestyramine	Hyperlipidemia	Chol 315 mg/dl, 60–65 yr old	Oster and Epstein (51)	1987	1,055,000
Lovastatin (20 mg/d)	Hyperlipidemia	1°, chol ≥300 mg/dl, 0 RF, women 35–44 yr old	Goldman et al. (8)	1991	2,024,800

*Adapted with permission from Kupersmith J, Holmes-Rovner M, Hogan A, Rovner D, Gardiner J. Cost-effectiveness analyses in heart disease: ischemia, congestive heart failure, and arrhythmias. Prog Cardiovasc Dis 1995;37:307–48. †All values have been updated to 1993 $; values with a dagger are shown in dollars per quality-adjusted life years ($/QALY); those without a dagger are in dollars per year of life saved ($/YLS). ‡Fifty-five year old men with type A lesions and normal ventricular function. §Saves both money and lives or quality-adjusted life years. ‖Analysis was of 55-year old man; ejection fraction (EF) ≥0.40. #Lipid Research Clinics Trial-Coronary Primary Prevention Trial (LRC-CPPT), patients were men (average age 48 years), 38% smokers, cholesterol ≥265 mg/dl, low density lipoprotein ≥190 mg/dl. ¶Minimal willingness to pay; interventional strategy was coronary artery bypass graft surgery (CABG); percutaneous transluminal coronary angioplasty (PTCA) was not considered. **Fineberg et al. (49) data recalculated by Weinstein and Stason (19). CAD = coronary artery disease; CCU = coronary care unit; CHF = congestive heart failure; Chol = pretreatment cholesterol; d = day; DBP = diastolic blood pressure; ECG = electrocardiographic; Ex = exercise; MI = myocardial infarction; Pt = patient; ref = reference; RF = other risk factors; VD = vessel disease. 1° = primary prevention; 2° = secondary prevention.

less, league tables can provide a useful general approach. In such tables, the interventions are often ranked in terms of the cost per unit of effectiveness (usually years of life or quality-adjusted life years saved).

It is appealing to choose a dollar threshold for intervention; interventions whose cost-effectiveness ratio is less than this figure would be considered acceptable values, whereas those with greater cost-effectiveness ratios would be considered too expensive. Some interventions, such as therapy with inexpensive antihypertensive drugs, are cost-effective in nearly every population studied. Many other interventions are highly cost-effective in some but not all individuals with the targeted condition. For example, as Table 2 illustrates, low dose lovastatin is cost-saving when administered to middle-aged male survivors of myocardial infarction; costs about $4,700 per year of life saved when administered to middle-aged female survivors of myocardial infarction; and costs more than $2,000,000 per year of life saved when used for primary prevention in young women with hypercholesterolemia.

Although such tables provide useful information, their interpretation must recognize the characteristics and comparability of the studies on which they are based. Because league tables usually draw from multiple published studies, it is important to ensure that the components of the studies, as presented in the table, are comparable.

Studies commonly differ in the ways they measure costs and effectiveness, the way in which the intervention is defined and applied, assumptions about the underlying health care system into which the intervention is integrated and the population under study. The manner in which costs are measured (e.g., generated from charge data, actual payments or formulas designed to estimate "true" costs; comprehensiveness in including all appropriate costs; method for projecting future costs and adjusting for inflation) may differ among studies. Similarly, the units of effectiveness may vary (e.g., life expectancy, quality-adjusted life years or a more limited outcome, such as number of lives saved or test result). Even among studies that use quality-adjusted life years, the method for measuring quality of life may vary, with significant consequences for the estimated effectiveness of the intervention. Studies may also vary markedly in the extent to which they have performed sensitivity analyses to confirm the reliability of their conclusions. League tables constructed with attention to such considerations are most likely to be useful in estimating the relative value of alternative medical interventions.

The rare interventions that save costs as well as years of life obviously should be adopted, but most interventions represent a true financial investment to yield health rather than economic benefits. Some investigators have proposed that if the cost per year of life (or quality adjusted year of life) is less than about $20,000, the intervention is generally considered very cost effective, whereas progressively more costly interventions are less and less attractive. At the current time, programs that cost less than about $40,000 per year of life saved, which roughly correspond to renal dialysis, have been recommended by some authors. Conversely, at costs above about $75,000 per year of life saved, we find it difficult to generate enthusiasm for an intervention unless there are reasons to believe the analysis is not sufficiently comprehensive to represent the

clinical decision adequately. For intermediate-range costs, it is difficult to be prescriptive.

Conclusions

Based on these general guidelines, programs for smoking cessation, screening and treating hypertension, especially with low cost medications, and secondary prevention with aspirin and cholesterol-lowering are recommended. Cholesterol reduction for primary prevention is more problematic, with current analyses suggesting that it be targeted to patients whose risk is substantially elevated because of additional risk factors or markedly elevated cholesterol levels, and that lower cost medications be emphasized. Comprehensive cardiac rehabilitation after a myocardial infarction may also be worthwhile from a cost-effectiveness standpoint, although its incremental value when added to other cost-effective treatments is not certain.

The cost-effectiveness of a medical intervention depends not only on its inherent characteristics but also on the patients to whom it is applied. Cost-effectiveness ratios describe an interaction between an intervention and a patient. In the evaluation of specific strategies, the following issues should be considered:

1. What is the expected impact of an intervention on mortality and quality of life?
2. How high are the costs of the strategy compared with alternatives? Will these costs be offset by economic savings due to delays or prevention of adverse outcomes?
3. What is the time frame in which the costs and benefits are expected to occur?
4. How likely is your patient to adhere to the recommended therapy?

As reflected in research described in this task force, effective interventions that are well tolerated in high risk patients often have attractive cost-effectiveness ratios regardless of their initial costs. These same interventions may have much less favorable cost-effectiveness ratios when applied in low risk populations. These findings demonstrate the importance of the goal of this Bethesda Conference.

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References

1. Detsky AS, Naglie IG. A clinician's guide to cost-effectiveness analysis. Ann Intern Med 1990;113:147–54.
2. Kupersmith J, Holmes-Rovner M, Hogan A, Rovner D, Gardiner J. Cost-effectiveness analysis in heart disease. Part I: general principles. Prog Cardiovasc Dis 1994;37:161–84.
3. Garber AM, Littenberg B, Sox HC, Wagner JL, Gluck M. Costs and health consequences of cholesterol screening for asymptomatic older Americans. Arch Intern Med 1991;151:1089–95.
4. Goldman L. Quantitative aspects of clinical reasoning. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's Principles of Internal Medicine. 13th ed. New York: McGraw-Hill, 1994:43–8.
5. Goldman L. Cost awareness in medicine. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's Principles of Internal Medicine. 13th ed. New York: McGraw-Hill, 1994:38–42.
6. Pekkanen J, Linn S, Heiss G, et al. Ten-year mortality from cardiovascular disease in relation to cholesterol level among men with and without preexisting cardiovascular disease. N Engl J Med 1990;322:1700–7.
7. Cupples LA, D'Agostino RB. Survival following initial cardiovascular events: 30 year follow-up. In: Kannel WB, Wolf PA, Garrison, editors. The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease. Bethesda (MD): National Heart, Lung, and Blood Institute publication no. (NIH) 88-2; 1988, Section 38.
8. Goldman L, Weinstein MC, Goldman PA, Williams LW. Cost-effectiveness of HMG-CoA reductase inhibition for primary and secondary prevention of coronary heart disease. JAMA 1991;265:1145–51.
9. Goldman L, Goldman P, Williams L, Weinstein MC. Cost-effectiveness considerations in the treatment of heterozygous familial hypercholesterolemia with medications. Am J Cardiol 1993;72:75D.
10. Hamilton VH, Racicot FE, Zowall H, Coupal L, Grover SA. The cost-effectiveness of HMG-CoA reductase inhibitors to prevent coronary heart disease. Estimating the benefits of increasing HDL-C. JAMA 1995;273:1032–8.
11. Lindgren B, Perrson U. The cost-effectiveness of a new antihypertensive drug, doxazosin. Curr Ther Res 1989;45:738–60.
12. Abbott RD, McGee D, Kannel WB, Wolf PA, Garrison RJ. The probability of developing certain cardiovascular disease in eight years at specified values of some characteristics. In: The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease. 87-2nd ed. Bethesda (MD): US Dept. of Health, Education and Welfare; 1987, Section 37. Publications NIH 87:2284.
13. Silberberg JS. Estimating the benefits of cholesterol lowering: are risk factors for coronary heart disease multiplicative? J Clin Epidemiol 1990;43:875–9.
14. Cupples LA, D'Agostino RB. Some risk factors related to the annual incidence of cardiovascular disease and death using pooled repeated bienniel measurements: Framingham heart study, 30 year follow-up. In: Kannel WB, Wolf PA, Garrison, editors. The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease. Bethesda (MD): National Heart, Lung, and Blood Institute publication No. (NIH) 87-2703; 1987, Section 34.
15. Goldman L, Gordon DJ, Rifkind BM, et al. Cost and health implications of cholesterol lowering. Circulation 1991;85:1960–8.
16. Hay JW, Wittels EH, Gotto AM Jr. An economic evaluation of lovastatin for cholesterol lowering and coronary artery disease reduction. Am J Cardiol 1991;67:789–96.
17. Kinosian BP, Eisenberg JM. Cutting into cholesterol. Cost-effective alternatives for treating hypercholesterolemia. JAMA 1988;259:2249–54.
18. Oster G, Epstein AM. Cost-effectiveness of antihyperlipemic therapy in the prevention of coronary heart disease. The case of cholestyramine. JAMA 1987;258:2381–7.
19. Weinstein MC, Stason WB. Cost-effectiveness of interventions to prevent or treat coronary heart disease. Ann Rev Public Health 1985;6:41–63.
20. Grover SA, Abrahamowicz M, Joseph L, Brewer C, Coupal L, Suissa S. The benefits of treating hyperlipidemia to prevent coronary heart disease. Estimating changes in life expectancy and morbidity. JAMA 1992;267:816–22.
21. Littenberg B, Garber AM, Sox HC Jr. Screening for hypertension. Ann Intern Med 1990;112:192–202.
22. Weinstein MC, Stason WB. Hypertension: A Policy Perspective. Cambridge (MA): Harvard University Press, 1976.
23. Edelson JT, Weinstein MC, Tosteson ANA, Williams L, Lee TH, Goldman L. Long-term cost-effectiveness of various initial monotherapies for mild to moderate hypertension. JAMA 1990;263:407–13.
24. Tsevat J, Weinstein MC, Williams LW, Tosteson AN, Goldman L. Expected gains in life expectancy from various coronary heart disease risk factor modifications. Circulation 1991;83:1194–201.
25. Taylor WC, Pass TM, Shepard DS, Komaroff AL. Cholesterol reduction and life expectancy. A model incorporating multiple risk factors. Ann Intern Med 1987;106:605–14.
26. Kottke TE, Battista RN, DeFriese GH, Brekke ML. Attributes of successful smoking cessation interventions in medical practice. A meta-analysis of 39 controlled trials. JAMA 1988;259:2883–9.
27. Cummings SR, Rubin SM, Oster G. The cost-effectiveness of counseling smokers to quit. JAMA 1989;261:75–9.
28. Oster G, Huse DM, Delea TE, Colditz GA. Cost-effectiveness of nicotine

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gum as an adjunct to physician's advice against cigarette smoking. JAMA 1986;256:1315–8.
29. Tsevat J. Impact and cost-effectiveness of smoking interventions. Am J Med 1992;93:43S–7S.
30. Krumholz HM, Cohen BJ, Tsevat J, Pasternak RC, Weinstein MC. Cost-effectiveness of a smoking cessation program after myocardial infarction. J Am Coll Cardiol 1993;22:1697–702.
31. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. JAMA 1988;260:945–50.
32. O'Connor GT, Buring JE, Yusuf S, et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989; 80:234–44.
33. Oldridge N, Furlong W, Feeny D, et al. Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction. Am J Cardiol 1993;72: 154–61.
34. Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol 1990;132:612–28.
35. Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. N Engl J Med 1988;319:1173–9.
36. Arroll B, Beaglehole R. Does physical activity lower blood pressure: a critical review of the clinical trials. J Clin Epidemiol 1992;45:439–47.
37. Consensus Development Conference on Diet and Exercise in Non-Insulin-Dependent Diabetes Mellitus. National Institutes of Health. Diabetes Care 1987;10:639–44.
38. Wood PD, Stefanick ML, Williams PT, Haskell WL. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. N Engl J Med 1991;325:461–6.
39. Grady D, Rubin SM, Petitti DB, et al. Hormone therapy to prevent disease and prolong life in postmenopausal women. Ann Intern Med 1992;117: 1016–37.
40. Tosteson AN, Rosenthal DI, Melton LJ, Weinstein MC. Cost effectiveness of screening perimenopausal white women for osteoporosis: bone densitometry and hormone replacement therapy. Ann Intern Med 1990;113:594–603.
41. Cairns JA, Markham BA. Economics and efficacy in choosing oral anticoagulants or aspirin after myocardial infarction. JAMA 1995;273:965
42. Glick H, Cook J, Bourassa M, et al. Projections of the costs and benefits of enalapril treatment in patients with symptomatic heart failure [abstract]. J Am Coll Cardiol 1994;23:284A.
43. Goldman L, Sia STB, Cook EF, Rutherford JD, Weinstein MC. Costs and effectiveness of routine therapy with long-term beta-adrenergic antagonists after acute myocardial infarction. N Engl J Med 1988;319:152–7.
44. Wong JB, Sonnenberg FA, Salem DN, Pauker SG. Myocardial revascularization for chronic stable angina: Analysis of the role of percutaneous transluminal coronary angioplasty based on data available in 1989. Ann Intern Med 1990;113:852–71.
45. Weinstein MC, Stason WB. Cost-effectiveness of coronary artery disease. Circulation 1982;66 Suppl III:III-56–66.
46. Hatziandreu EI, Koplan JP, Weinstein MC, Caspersen CJ, Warner KE. A cost-effectiveness analysis of exercise as a health promotion activity. Am J Public Health 1988;78:1417–21.
47. Tsevat J, Duke D, Goldman L, et al. Cost-effectiveness of captopril therapy after myocardial infarction. J Am Coll Cardiol 1995;26:914–9.
48. Doubilet P, McNeil BJ, Weinstein MC. The decision concerning coronary angiography in patients with chest pain: a cost-effectiveness analysis. Med Decis Making 1985;5:293–309.
49. Fineberg HV, Scadden D, Goldman L. Care of patients with a low probability of acute myocardial infarction: cost effectiveness of alternatives to coronary-care-unit admission. N Engl J Med 1984;310:1301–7.
50. Sox HC, Blatt MA, Higgins MC, Marton KI. Medical Decision Making. Stoneham (MA): Butterworth, 1988.
51. Oster G, Epstein AM. Primary prevention and coronary heart disease: the economic benefits of lowering serum cholesterol. Am J Public Health 1986;76:647–56.

Task Force 7. Evaluation and Management of Risk Factors for the Individual Patient (Case Management)

H. J. C SWAN, MD, PHD, FACC, CHAIR, BERNARD J. GERSH, MB, CHB, DPHIL, FRCP, FACC, THOMAS B. GRABOYS, MD, FACC, DANIEL J. ULLYOT, MD, FACC

Several factors that increase risk for atherosclerosis in general, and coronary disease in particular, have been identified and are generally accepted in medical practice as valid and relevant (1). These include cigarette smoking, sedentary life-style, hypertension, abnormal blood lipid levels and a thrombogenic tendency, among others. However, conclusive evidence from population-based studies of reduction of all-cause mortality by modification of such risk factors has been lacking (2-4). Nevertheless, significant (although modest) reduction in coronary artery disease (CAD) mortality and morbidity has been found in these population studies. This benefit is greatest in patients with evidence of coronary disease, or in studies in which the control subjects are at a mortality risk of 4% or greater per year (5,6).

The term prevention—"primary" or "secondary"—is widely used to encompass reduction of these common risk factors in normal persons or in patients with coronary heart disease, respectively. "Primary prevention" implies becoming a non-smoker, maintaining a normal blood pressure and a desirable body weight and consuming no more than 10% of calories from saturated fat. In these healthy people, behavior modification, diet and exercise programs are designed to promote a healthy life-style. Also, these measures will allow some people to avoid or delay the development of atherosclerosis. "Secondary prevention" relates to the treatment of coronary artery disease in patients who have had a clinical event (for example, angina pectoris or acute myocardial infarction) by reduction of conventional risk factors but also includes the use of cardio-